etaine hostïguest complexation with a calixarene receptor: enhanced in vitro anticancer effectÀ

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Abstract

p-Sulfonatocalix[n]arenes have shown excellent potential for accommodating chemotherapeutic drugs through hostïguest complexation and enhancing their anticancer activity. Betaine has been reported to exert an anticancer effect at high concentrations. In order to increase its concentration in cancer cells, we have complexed it with p-SC4, which releases its content in an acidic environment typical of cancer tissue. In this work, a hostïguest complex of the chemically stable, natural, and safe active methyl donor (betaine) and p-sulfonatocalix[4]arenes (p-SC4) was designed and characterized using 1H NMR, UV, Job's plot analysis, DFT calculations, and molecular modeling for use in cancer therapeutics. The peak amplitude of the prepared hostïguest complexes was linearly proportional to the concentration of betaine in the range of 1.0 Ǐ 10ī5 Mī1 to 2.5 Ǐ 10ī4 Mī1. The reaction stoichiometry between p-SC4 and betaine in the formed complex was 1[thin space (1/6-em)]:[thin space (1/6-em)]1. The stability constant for the complex is 8.9 Ǐ 104 Mī1 which corresponds to a complexation free energy of ī6.74 kcal molī1. Complexation between betaine and p-SC4 was found to involve the insertion of the trimethylammonium group of betaine into the p-SC4 cavity, as supported by the experimental data. The complex displayed enhanced cytotoxic activities against breast adenocarcinoma cells (MCF-7) and cervical cancer cells (HeLa) compared to free betaine. In conclusion, the hostïguest complexation of betaine with p-SC4 increases its concentration in cancer cells, which warrants further investigation for cancer therapy.

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